

Claims

1. An agent for treating an inflammatory bowel disease comprising a combination of (a) at least one compound having an anti-inflammatory action and being selected from the group consisting of an aminosalicylic acid derivative, an anti-inflammatory glucocorticoid, a compound having an immunosuppressive action, an anti-TNF $\alpha$  antibody, a pituitary hormone and a compound having an anti-infective action as an active ingredient and (b) at least one compound having a PPAR $\gamma$  agonistic action as an active ingredient, wherein the agent is so configured that the compound (a) and the compound (b) are used simultaneously, separately or every scheduled time.

2. An agent for treating an inflammatory bowel disease comprising a combination of (a) at least one compound having an anti-inflammatory action and being selected from the group consisting of an aminosalicylic acid derivative, an anti-inflammatory glucocorticoid, a compound having an immunosuppressive action and an anti-TNF $\alpha$  antibody as an active ingredient and (b) at least one compound having a PPAR $\gamma$  agonistic action as an active ingredient, wherein the agent is so configured that the compound (a) and the compound (b) are used simultaneously, separately or every scheduled time.

3. An agent for treating an inflammatory bowel

disease comprising a combination of (a) at least one compound having an anti-inflammatory action and being selected from the group consisting of an aminosalicylic acid derivative and a compound having an immunosuppressive action as an active ingredient and (b) at least one compound having a PPAR $\gamma$  agonistic action as an active ingredient, wherein the agent is so configured that the compound (a) and the compound (b) are used simultaneously, separately or every scheduled time.

4. The agent for treating an inflammatory bowel disease according to claim 1, wherein the compound having a PPAR $\gamma$  agonistic action is a compound having a PPAR $\gamma$  agonistic action for use in leukocytapheresis treatment or granulocytapheresis treatment.

5. The agent for treating an inflammatory bowel disease according to any one of claims 1 to 4, wherein the compound having a PPAR $\gamma$  agonistic action is a compound selected from the group consisting of:

- (1) 2-isopropoxy-3-[3-([4-(trifluoromethyl)benzyl]-oxyethanimidoyl)phenyl]propanoic acid,
- (2) 3-{3-[3-(2,4-dichlorophenoxy)-2(S)-hydroxypropoxy]phenyl}-2(S)-isopropoxypropanoic acid,
- (3) 3-(3-{2(R)-hydroxy-3-[4-chlorophenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid,
- (4) 3-{3-[3-(2,4-dichlorophenoxy)-2(R)-hydroxypropoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(5) 3-{3-[3-(2,4-dichlorophenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(6) 3-{3-[3-(4-chlorophenoxy)-2(S)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(7) 3-{3-[3-(4-chloro-2-cyanophenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(8) 3-{3-[3-(2,4-dichlorophenoxy)-2(S)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(9) 3-{3-[3-(4-chlorophenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(10) 3-{3-[3-(4-chloro-2-cyanophenoxy)-2(S)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(11) 2(S)-isopropoxy-3-{3-[ (4-trifluoromethylbenzyloxycarbonylamino)methyl]phenyl}-propanoic acid,

(12) 2(S)-isopropoxy-3-{3-[ (3-trifluoromethylbenzyloxycarbonylamino)methyl]phenyl}-propanoic acid,

(13) 2(S)-isopropoxy-3-{3-[ (4-trifluoromethoxybenzyloxycarbonylamino)methyl]phenyl}-propanoic acid,

(14) 3-(3-{ [3-trifluoromethoxybenzyloxycarbonylamino]-methyl}phenyl)-2(S)-isopropoxypropanoic acid,

(15) 3-{ [3-(2,4-dichlorophenyl)carbamoyloxyethyl-4-ethoxy]phenyl}-2-isopropoxypropanoic acid,

(16) 3-({4-[5-(benzo[1,3]dioxolyl)]carbamoyloxyethyl}-

phenyl)-2-isopropoxypropanoic acid,

(17) 3-{3-[3-(4-chlorophenyl)-2-propynloxy]phenyl}-2(S)-isopropoxypropanoic acid,

(18) 3-{[3-(2,4-dichlorophenyl)carbamoyloxymethyl-4-ethoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(19) 3-(3-{2(R)-hydroxy-3-[2-bromo-4-methylphenoxy]-propoxy}phenyl)-2(S)-isopropoxypropanoic acid,

(20) 3-{[4-(4-ethoxyphenyl)carbamoyloxymethyl]phenyl}-2-isopropoxypropanoic acid,

(21) 2-isopropoxy-3-[4-(2-{[4-(trifluoromethyl)phenyl]-carbamoyloxy}ethyl)phenyl]propanoic acid,

(22) 3-[3-([2,4-dichlorobenzoyl]aminomethyl)-4-methoxyphenyl]-2(S)-isopropoxypropanoic acid,

(23) 3-[3-([2-fluoro-4-(trifluoromethyl)benzoyl]-aminomethyl)-4-methoxyphenyl]-2(S)-isopropoxypropanoic acid,

(24) 2-ethoxy-3-(2-{2-[4-(trifluoromethyl)phenoxy]ethoxy}-4-pyridyl)propanoic acid,

(25) 3-(2-{2-[4-(tert-butyl)phenoxy]ethoxy}-4-pyridyl)-2-ethoxypropanoic acid,

(26) 3-(3-[(2-chloro-4-propoxybenzoyl)amino]methyl-2,4-dimethoxyphenyl)-2-isopropoxypropanoic acid,

(27) 3-(7-[(2,4-dichlorobenzoyl)amino]methylbenzo[b]furan-5-yl)-2-isopropoxypropanoic acid,

(28) 3-(7-[(2-chloro-4-propoxybenzoyl)amino]methyl-2,3-dihydrobenzo[b]furan-5-yl)-2-isopropoxypropanoic acid,

(29) 2-(3-[(2-chloro-4-propoxybenzoyl)amino]methyl)-4-

ethoxybenzyl)tetrahydro-2-furancarboxylic acid,  
(30) 2-(3-{[(2-chloro-4-propoxybenzoyl)amino]methyl}-4-ethoxybenzyl)tetrahydro-2-furancarboxylic acid,  
(31) pioglitazone,  
(32) netoglitazone,  
(33) tesaglitazar,  
(34) 5-(2,4-dioxothiazolidin-5-ylmethyl)-2-methoxy-N-(4-trifluoromethylbenzyl)benzamide,  
(35) 5-[4-(6-methoxy-1H-benzimidazol-2-ylmethoxy)benzyl]-thiazolidine-2,4-dione,  
(36) 4-[4-(5-methyl-2-phenyloxazol-4-ylmethoxy)-benzyloxyimino]-4-phenylbutyric acid and  
(37) (4-methoxyphenoxy carbonyl-[4-[2-(5-methyl-2-phenyloxazol-4-yl)ethoxy]benzyl]amino)acetic acid,  
a salt thereof or a hydrate of them.

6. The agent for treating an inflammatory bowel disease according to any one of claims 1 to 4, wherein the compound having a PPAR $\gamma$  agonistic action is a compound selected from the group consisting of:

- (1) 2-isopropoxy-3-[3-([4-(trifluoromethyl)benzyl]-oxyethanimidoyl)phenyl]propanoic acid,
- (2) 3-{3-[3-(2,4-dichlorophenoxy)-2(R)-fluoro-propoxy]phenyl}-2(S)-isopropoxypropanoic acid,
- (3) 3-{3-[3-(4-chlorophenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid,
- (4) 3-{3-[3-(4-chloro-2-cyanophenoxy)-2(S)-

fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(5) 2(S)-isopropoxy-3-{3-[4-trifluoromethoxybenzyloxycarbonylamino)methyl]phenyl}-propanoic acid,

(6) 3-(3-{[3-trifluoromethoxybenzyloxycarbonylamino]-methyl}phenyl)-2(S)-isopropoxypropanoic acid,

(7) pioglitazone,

(8) netoglitazone,

(9) tesaglitazar,

(10) 5-(2,4-dioxothiazolidin-5-ylmethyl)-2-methoxy-N-(4-trifluoromethylbenzyl)benzamide,

(11) 5-[4-(6-methoxy-1H-benzimidazol-2-ylmethoxy)benzyl]-thiazolidine-2,4-dione,

(12) 4-[4-(5-methyl-2-phenyloxazol-4-ylmethoxy)-benzyloxyimino]-4-phenylbutyric acid and

(13) (4-methoxyphenoxy carbonyl-[4-[2-(5-methyl-2-phenyloxazol-4-yl)ethoxy]benzyl]amino)acetic acid,  
a salt thereof or a hydrate of them.

7. The agent for treating an inflammatory bowel disease according to any one of claims 1 to 4, wherein the compound having a PPAR $\gamma$  agonistic action is a compound selected from the group consisting of:

(1) 2-isopropoxy-3-{3-([4-(trifluoromethyl)benzyl]-oxyethanimidoyl)phenyl]propanoic acid,

(2) 3-{3-[3-(2,4-dichlorophenoxy)-2(S)-hydroxypropoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(3) 3-(3-{2(R)-hydroxy-3-[4-chlorophenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid,

(4) 3-{3-[3-(2,4-dichlorophenoxy)-2(R)-hydroxypropoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(5) 3-{3-[3-(2,4-dichlorophenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(6) 3-{3-[3-(4-chlorophenoxy)-2(S)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(7) 3-{3-[3-(4-chloro-2-cyanophenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(8) 3-{3-[3-(2,4-dichlorophenoxy)-2(S)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(9) 3-{3-[3-(4-chlorophenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(10) 3-{3-[3-(4-chloro-2-cyanophenoxy)-2(S)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(11) 2(S)-isopropoxy-3-{3-[4-trifluoromethylbenzyloxycarbonylamino)methyl]phenyl}-propanoic acid,

(12) 2(S)-isopropoxy-3-{3-[3-trifluoromethylbenzyloxycarbonylamino)methyl]phenyl}-propanoic acid,

(13) 2(S)-isopropoxy-3-{3-[4-trifluoromethoxybenzyloxycarbonylamino)methyl]phenyl}-propanoic acid,

(14) 3-(3-{[3-trifluoromethoxybenzyloxycarbonylamino]-

methyl}phenyl)-2(S)-isopropoxypropanoic acid,

(15) 3-{{3-(2,4-dichlorophenyl)carbamoyloxymethyl-4-ethoxy]phenyl}-2-isopropoxypropanoic acid,

(16) 3-({4-[5-(benzo[1,3]dioxolyl)]carbamoyloxymethyl}-phenyl)-2-isopropoxypropanoic acid,

(17) 3-{3-[3-(4-chlorophenyl)-2-propynyloxy]phenyl}-2(S)-isopropoxypropanoic acid,

(18) 3-{{3-(2,4-dichlorophenyl)carbamoyloxymethyl-4-ethoxy]phenyl}-2(S)-isopropoxypropanoic acid,

(19) 3-(3-{2(R)-hydroxy-3-[2-bromo-4-methylphenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid,

(20) 3-{{4-(4-ethoxyphenyl)carbamoyloxymethyl}phenyl}-2-isopropoxypropanoic acid,

(21) 2-isopropoxy-3-[4-(2-{{4-(trifluoromethyl)phenyl}-carbamoyloxy}ethyl)phenyl]propanoic acid,

(22) 3-[3-({2,4-dichlorobenzoyl}aminomethyl)-4-methoxyphenyl]-2(S)-isopropoxypropanoic acid,

(23) 3-[3-({2-fluoro-4-(trifluoromethyl)benzoyl}-aminomethyl)-4-methoxyphenyl]-2(S)-isopropoxypropanoic acid,

(24) 2-ethoxy-3-(2-{2-[4-(trifluoromethyl)phenoxy]ethoxy}-4-pyridyl)propanoic acid,

(25) 3-(2-{2-[4-(tert-butyl)phenoxy]ethoxy}-4-pyridyl)-2-ethoxypropanoic acid,

(26) 3-(3-[(2-chloro-4-propoxybenzoyl)amino]methyl-2,4-dimethoxyphenyl)-2-isopropoxypropanoic acid,

(27) 3-(7-[(2,4-dichlorobenzoyl)amino]methylbenzo[b]furan-

5-yl)-2-isopropoxypropanoic acid,  
(28) 3-(7-[(2-chloro-4-propoxybenzoyl)amino]methyl-2,3-dihydrobenzo[b]furan-5-yl)-2-isopropoxypropanoic acid,  
(29) 2-(3-[(2-chloro-4-propoxybenzoyl)amino]methyl)-4-ethoxybenzyl)tetrahydro-2-furancarboxylic acid and  
(30) 2-(3-[(2-chloro-4-propoxybenzoyl)amino]methyl)-4-ethoxybenzyl)tetrahydro-2-furancarboxylic acid,  
a salt thereof or a hydrate of them.

8. The agent for treating an inflammatory bowel disease according to any one of claims 1 to 4, wherein the compound having a PPAR $\gamma$  gonistic action is a compound selected from the group consisting of:

- (1) 2-isopropoxy-3-[3-([4-(trifluoromethyl)benzyl]-oxyethanimidoxy)phenyl]propanoic acid,
- (2) 3-{3-[3-(2,4-dichlorophenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid,
- (3) 3-{3-[3-(4-chlorophenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid,
- (4) 3-{3-[3-(4-chloro-2-cyanophenoxy)-2(S)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid,
- (5) 2(S)-isopropoxy-3-{3-[(4-trifluoromethoxybenzyloxycarbonylamino)methyl]phenyl}-propanoic acid and
- (6) 3-(3-[(3-trifluoromethoxybenzyloxycarbonylamino)methyl]phenyl)-2(S)-isopropoxypropanoic acid, a salt thereof or a hydrate of them.

9. The agent for treating an inflammatory bowel disease according to any one of claims 1 to 4, wherein the compound having a PPAR $\gamma$  agonistic action is 3-[3-[4-chloro-2-cyanophenoxy]-2(S)-fluoropropoxy]phenyl]-2(S)-isopropoxypropanoic acid, a salt thereof or a hydrate of them.

10. The agent for treating an inflammatory bowel disease according to any one of claims 1 to 3, wherein the aminosalicylic acid derivative is:

- (1) sulfasalazine,
- (2) mesalazine,
- (3) olsalazine or
- (4) balsalazide.

11. The agent for treating an inflammatory bowel disease according to claim 1 or 2, wherein the anti-inflammatory glucocorticoid is:

- (1) prednisolone,
- (2) betamethasone,
- (3) hydrocortisone,
- (4) cortisone acetate,
- (5) methylprednisolone,
- (6) prednisone or
- (7) budesonide.

12. The agent for treating an inflammatory bowel disease according to any one of claims 1 to 3, wherein the compound having an immunosuppressive action is:

- (1) cyclosporin,
- (2) azathioprine,
- (3) 6-mercaptopurine,
- (4) tacrolimus or
- (5) methotrexate.

13. The agent for treating an inflammatory bowel disease according to claim 1 or 2, wherein the anti-TNF $\alpha$  antibody is an antibody contained in:

- (1) infliximab,
- (2) etanercept,
- (3) CDP-571,
- (4) adalimumab or
- (5) CDP-870.

14. The agent for treating an inflammatory bowel disease according to claim 1, wherein the compound having an anti-infective action is:

- (1) metronidazole,
- (2) clarithromycin,
- (3) tobramycin,
- (4) ciprofloxacin hydrochloride,
- (5) ampicillin,
- (6) cefazolin,
- (7) ofloxacin or
- (8) levofloxacin.

15. The agent for treating an inflammatory bowel disease according to claim 1, wherein the pituitary hormone

is tetracosactide acetate.

16. The agent for treating an inflammatory bowel disease according to claim 2, wherein the group consisting of an aminosalicylic acid derivative, an anti-inflammatory glucocorticoid, a compound having an immunosuppressive action and an anti-TNF $\alpha$  antibody is the group consisting of sulfasalazine, mesalazine, prednisolone, betamethasone, hydrocortisone, cortisone acetate, methylprednisolone, prednisone, cyclosporin and tacrolimus.

17. The agent for treating an inflammatory bowel disease according to claim 3, wherein one compound having an anti-inflammatory action and being selected from the group consisting of an aminosalicylic acid derivative and a compound having an immunosuppressive action is sulfasalazine or cyclosporin.

18. An agent for treating an inflammatory bowel disease, which comprises a combination of (a) a compound having an anti-inflammatory action and being selected from the group consisting of sulfasalazine and cyclosporin as an active ingredient and (b) a compound having a PPAR $\gamma$  agonistic action and being 3-[3-[3-(4-chloro-2-cyanophenoxy)-2(S)-fluoropropoxy]phenyl]-2(S)-isopropoxypropanoic acid, a salt thereof or a hydrate of them as an active ingredient, wherein the agent is so configured that the compound (a) and the compound (b) are used simultaneously, separately or every scheduled time.

19. The agent according to any one of claims 1 to 17, wherein the inflammatory bowel disease is ulcerative colitis.

20. The agent according to any one of claims 1 to 17, wherein the inflammatory bowel disease is Crohn's disease.

21. An agent for treating an inflammatory bowel disease, which comprises a combination of the compound (a) and the compound (b) as described in claim 1.

22. The agent according to claim 21, wherein the combination of the compound (a) and the compound (b) is simultaneous or separate administration.

23. The agent according to claim 21, wherein the combination of the compound (a) and the compound (b) is successive administration.

24. Use of the combination of the compound (a) and the compound (b) as described in claim 1, for producing an agent for treating an inflammatory bowel disease.

25. The use according to claim 24, wherein the combination of the compound (a) and the compound (b) is simultaneous or separate administration.

26. The use according to claim 24, wherein the combination of the compound (a) and the compound (b) is administration every scheduled time.

27. A method for treating an inflammatory bowel disease, which comprises administering a pharmacologically effective amount of the combination of the compound (a) and

the compound (b) described in claim 1 to a patient.

28. The method according to claim 27, which comprises administering the compound (a) and the compound (b) simultaneously or separately to the patient.

29. The method according to claim 27, which comprises administering the compound (a) and the compound (b) every scheduled time to the patient.